

What is claimed is:

1. Crystalline cPLA2.
2. The crystalline cPLA2 of claim 1 wherein said cPLA2 is human cPLA2.
3. The crystalline cPLA2 of claim 1 wherein said cPLA2 is cPLA2 from a non-mammalian species.
4. The crystalline cPLA2 of claim 1 wherein said cPLA2 is recombinant cPLA2.
5. The crystalline cPLA2 of claim 1 wherein said cPLA2 comprises the mature sequence of naturally-occurring cPLA2.
6. A crystalline composition comprising cPLA2 in association with a second chemical species.
7. The composition of claim 6 wherein said second chemical species is selected from the group consisting of a potential inhibitor of cPLA2 activity and a potential inhibitor of cPLA2 binding.
8. A model of the structure of cPLA2 comprising a data set embodying the structure of cPLA2.
9. The model of claim 8 wherein said data set was determined by crystallographic analysis of cPLA2.

10. The model of claim 8 wherein said data set was determined by NMR analysis of cPLA2.

11. The model of claim 8 wherein said data set embodies the entire structure of cPLA2.

12. The model of claim 8 wherein said data set embodies a portion of the structure of cPLA2.

13. The model of claim 12 wherein said portion is the active site of cPLA2.

14. The model of claim 12 wherein said portion is the CaLB domain of cPLA2.

15. A computer system comprising computer hardware and the model of claim 8.

16. A method of identifying a species which is an agonist or antagonist of cPLA2 activity or binding comprising: (a) providing the model of claim 8, (b) studying the interaction of candidate species with such model, and (c) selecting a species which is predicted to act as said agonist or antagonist.

17. A species identified in accordance with the method of claim 16.

18. A process of identifying a substance that inhibits cPLA2 activity or binding comprising determining the interaction between a candidate substance and a model of the structure of cPLA2.

19. A process of identifying a substance that mimics cPLA2 activity or binding comprising determining the interaction between a candidate substance and a model of the structure of cPLA2.

20. A method of identifying inhibitors of cPLA2 activity by rational drug design comprising:

(a) designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the cPLA2 active site based upon the crystal structure co-ordinates of cPLA2;

(b) synthesizing the inhibitor; and

(c) determining whether the potential inhibitor inhibits the activity of cPLA2.

21. The method of claim 20 wherein the crystal structure co-ordinates of cPLA2 are obtained from a cPLA2 crystal of space group P2₁2₁2 with a = 153.59 angstroms, b = 95.49 angstroms, and c = 139.13 angstroms.

22. The method of claim 20 wherein said inhibitor is designed to interact with one or more atoms of said one or more amino acids in the cPLA2 active site, and wherein said one or more atoms is selected from the group consisting of:

CB and O γ atoms of Ser228;

O δ 1 and O δ 2 atoms of Asp549 and Asp575;

CB, CG, CD, NE, CZ, NH1 and NH2 atoms of Arg200, Arg413 and Arg579;

Backbone carbonyl oxygen of Trp393;

N δ 2 and O δ 1 atoms of Asn555;

Atoms CD1, CE1, CG, CZ, CE2, and CD2 of Phe397, Phe681, Phe683 and Phe199;

CG, CD1, NE1, CE2, CZ2, CH2, CZ3, CE3 and CD2 of Trp232
and Trp393;

CB and O γ atoms of Ser577;

Atom s CB and S γ of Cys331;

Atoms OE1 and OE2 of Glu589;

Atoms CB, CG, CD, CE and NZ of Lys588;

O γ 1 atom of Thr680;

OE1 and OE2 atoms of Glu418 and Glu422;

Atoms CB, CG, SD and CE of Met417;

Atoms CB, CG, CD1 and CD2 of Leu400 and Leu421;

Atoms CB, CG1, CG2, or CD1 of Ile424;

Backbone NH and carbonyl oxygen atoms of Ala578; and

Atoms CB, CG, ND1, CE1, NE2, and CD2 of His639.

23. A method of identifying inhibitors of cPLA2 membrane binding by rational drug design comprising:

(a) designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the cPLA2 electrostatic patch region based upon the crystal structure co-ordinates of cPLA2;

(b) synthesizing the inhibitor; and

(c) determining whether the potential inhibitor inhibits the membrane binding of cPLA2.

24. The method of claim 23 wherein the crystal structure co-ordinates of cPLA2 are obtained from a cPLA2 crystal of space group P2₁2₁2 with a = 153.59 angstroms, b = 95.49 angstroms, and c = 139.13 angstroms.

25. The method of claim 23 wherein said one or more amino acids are selected from the group consisting of Arg467, Arg485, Lys488, Lys544 and Lys543.

26. An agonist or antagonist identified by the method of claim 20.

27. An agonist or antagonist identified by the method of claim 23.

28. A substance identified by the method of claim 18.

29. A substance identified by the method of claim 19.

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